10/774,082 Restriction Search L/Cook 9/19/06

## d his

(FILE 'HOME' ENTERED AT 09:53:41 ON 19 SEP 2006)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 09:53:59 ON 19 SEP 2006

L1	2893	S (ANTIBOD? PURIF?)
L2	6	S L1 AND (NET CHARGE)
L3	327	S L1 AND PH
L4	17	S L3 AND ISOELECTRIC?
L5	0	S L4 AND L2
L6	258	DUPLICATE REMOVE L3 (69 DUPLICATES REMOVED)
L7	258	S L6 AND PH
L8	0	S L2 AND PH
L9	3	DUPLICATE REMOVE L2 (3 DUPLICATES REMOVED)
L10	17	DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

ANSWER 1 OF 3 • CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:187960 CAPLUS

DN 133:16029

ED Entered STN: 23 Mar 2000

- TI Development of ion exchange chromatography methods for monoclonal antibodies
- AU Bai, L.; Burman, S.; Gledhill, L.
- CS Analytical Sciences Department, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, USA
- SO Journal of Pharmaceutical and Biomedical Analysis (2000), 22(3), 605-611 CODEN: JPBADA; ISSN: 0731-7085
- PB Elsevier Science B.V.
- DT Journal
- LA English
- CC 15-1 (Immunochemistry)
- Monoclonal antibodies (MAbs) have been widely developed as AB biopharmaceutical agents to treat a number of diseases, such as asthma, arthritis, cancers, and multiple sclerosis, etc. MAbs are often found existing in multiple iso-forms with different net charges. These isoforms are evident as multiple bands on isoelec. focusing (IEF) gel anal. To isolate and study isoforms of proteins and monitor their distributions, many different techniques, such as slab gel electrophoresis, capillary electrophoresis (CE), ion exchange chromatog. (IEC), and hydrophilic interaction chromatog. (HIC) have been used. Compared with the other techniques, IEC has a larger selection of com. columns and is a potential nondenaturing preparative procedure to isolate the isoforms for subsequent characterization. However, due to the large mol. size of MAbs, successful separation of isoforms of MAbs by IEC is not often seen in publications. In this report the authors describe a systematic approach to develop IEC methods for MAbs. The authors used high efficient exchange resin, smaller internal diameter columns, and higher flow rate to achieve fast and high degree separation
- ST monoclonal antibody purifn ion exchange chromatog; charge isoform antibody ion exchange chromatog
- IT Immunoglobulins
  - RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (G1, monoclonal; purification and charge characterization of monoclonal antibodies by ion exchange chromatog.)
- IT Immunoglobulins
  - RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (G4, monoclonal; purification and charge characterization of monoclonal antibodies by ion exchange chromatog.)
- IT Ion exchange chromatography
  - (for purification and charge characterization of monoclonal antibodies)
- IT 271798-33-5, Bio-Scale S 2 271798-84-6, Mini S-PE
  - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(for purification and charge characterization of monoclonal antibodies by ion exchange chromatog.)

- RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
- (1) Anon; Federal Register 63 (1996) 31506-31513
- (2) Artigues, A; J Biol Chem 1990, V265, P4853 CAPLUS
- (3) Aswad, D; Deamidation and Isoaspartate Formation in Peptides and Proteins 1995
- (4) Bonger, J; Int J Pept Protein Res 1992, V39, P364
- (5) Cacia, J; Biochemistry 1996, V35, P1897 CAPLUS
- (6) Cacia, J; J Chromatogr 1993, V634, P229 CAPLUS
- (7) Denton, K; J Chromatogr B 1997, V697, P111 CAPLUS
- (8) Donato, A; J Biol Chem 1993, V268, P4745
- (9) Huang, T; Chromatographia 1994, V39, P543 CAPLUS
- (10) Hunt, G; J Chromatogr A 1996, V744, P295 CAPLUS
- (11) Kaltenbrunner, O; J Chromatogr 1993, V639, P41 CAPLUS
- (12) Kwong, M; Protein Sci 1994, V3, P147 CAPLUS

1 date good

- (13) Lee, H; J Chromatogr A 1997, V790, P215 CAPLUS
- (14) Liu, Q; J Liq Chromatogr Rel Technol 1997, V20, P707 CAPLUS
- (15) Moorhouse, K; J Pharm Biomed Anal 1997, V16, P593 CAPLUS
- (16) Righetti, P; J Chromatogr 1981, V220, P115 CAPLUS
- (17) Shahrokh, Z; Pharm Res 1994, V11, P936 CAPLUS
- (18) Tang, S; J Pharm Biomed Anal 1999, V19, P569 CAPLUS
- (19) Teshima, G; Biochemistry 1991, V30, P3916 CAPLUS
- (20) Teshima, G; J Biol Chem 1991, V266, P13544 CAPLUS
- (21) Wu, S; J Chromatogr 1990, V516, P115 CAPLUS
- (22) Yang, Y; J Chromatogr A 1996, V743, P171 CAPLUS

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN 2000:187960 CAPLUS ANDN ED Entered STN: 23 Mar 2000 Development of ion exchange chromatography methods for monoclonal ΤI antibodies Bai, L.; Burman, S.; Gledhill, L. ΑU Analytical Sciences Department, SmithKline Beecham Pharmaceuticals, King CS of Prussia, PA, USA Journal of Pharmaceutical and Biomedical Analysis (2000), 22(3), 605-611 SO CODEN: JPBADA; ISSN: 0731-7085 Elsevier Science B.V. PB DT Journal LA English 15-1 (Immunochemistry) CC Monoclonal antibodies (MAbs) have been widely developed as AΒ biopharmaceutical agents to treat a number of diseases, such as asthma, arthritis, cancers, and multiple sclerosis, etc. MAbs are often found existing in multiple iso-forms with different net charges. These isoforms are evident as multiple bands on isoelec. focusing (IEF) gel anal. To isolate and study isoforms of proteins and monitor their distributions, many different techniques, such as slab gel electrophoresis, capillary electrophoresis (CE), ion exchange chromatog. (IEC), and hydrophilic interaction chromatog. (HIC) have been used. Compared with the other techniques, IEC has a larger selection of com. columns and is a potential nondenaturing preparative procedure to isolate the isoforms for subsequent characterization. However, due to the large mol. size of MAbs, successful separation of isoforms of MAbs by IEC is not often seen in publications. In this report the authors describe a systematic approach to develop IEC methods for MAbs. The authors used high efficient exchange resin, smaller internal diameter columns, and higher flow rate to achieve fast and high degree separation monoclonal antibody purifn ion exchange chromatog; ST charge isoform antibody ion exchange chromatog IT Immunoglobulins RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (G1, monoclonal; purification and charge characterization of monoclonal antibodies by ion exchange chromatog.) IT Immunoglobulins RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (G4, monoclonal; purification and charge characterization of monoclonal antibodies by ion exchange chromatog.) IT Ion exchange chromatography (for purification and charge characterization of monoclonal antibodies) 271798-33-5, Bio-Scale S 2 271798-84-6, Mini S-PE IT RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (for purification and charge characterization of monoclonal antibodies by ion exchange chromatog.) RE.CNT THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Anon; Federal Register 63 (1996) 31506-31513 (2) Artigues, A; J Biol Chem 1990, V265, P4853 CAPLUS (3) Aswad, D; Deamidation and Isoaspartate Formation in Peptides and Proteins (4) Bonger, J; Int J Pept Protein Res 1992, V39, P364 (5) Cacia, J; Biochemistry 1996, V35, P1897 CAPLUS

(6) Cacia, J; J Chromatogr 1993, V634, P229 CAPLUS(7) Denton, K; J Chromatogr B 1997, V697, P111 CAPLUS

(9) Huang, T; Chromatographia 1994, V39, P543 CAPLUS(10) Hunt, G; J Chromatogr A 1996, V744, P295 CAPLUS

(12) Kwong, M; Protein Sci 1994, V3, P147 CAPLUS

(11) Kaltenbrunner, O; J Chromatogr 1993, V639, P41 CAPLUS

(8) Donato, A; J Biol Chem 1993, V268, P4745

- (13) Lee, H; J Chromatogr A 1997, V790, P215 CAPLUS
- (14) Liu, Q; J Liq Chromatogr Rel Technol 1997, V20, P707 CAPLUS
- (15) Moorhouse, K; J Pharm Biomed Anal 1997, V16, P593 CAPLUS
- (16) Righetti, P; J Chromatogr 1981, V220, P115 CAPLUS
- (17) Shahrokh, Z; Pharm Res 1994, V11, P936 CAPLUS
- (18) Tang, S; J Pharm Biomed Anal 1999, V19, P569 CAPLUS
- (19) Teshima, G; Biochemistry 1991, V30, P3916 CAPLUS
- (20) Teshima, G; J Biol Chem 1991, V266, P13544 CAPLUS
- (21) Wu, S; J Chromatogr 1990, V516, P115 CAPLUS
- (22) Yang, Y; J Chromatogr A 1996, V743, P171 CAPLUS

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ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN
     1992:103876 CAPLUS
DN
     116:103876
ED
     Entered STN: 20 Mar 1992
     Subsetting of acetylcholine receptor-reactive antibodies by preparative
ΤI
     isoelectric focusing
     Thompson, Patrica A.; Krolick, Keith A.
ΑU
     Health Sci. Cent., Univ. Texas, San Antonio, TX, 78284, USA
CS
     Preparative Biochemistry (1991), 21(4), 229-35
SO
     CODEN: PRBCBQ; ISSN: 0032-7484
DT
     Journal
     English
LΑ
CC
     15-1 (Immunochemistry)
     The antibodies produced against most foreign antigens are composed of a
AB
     family of Igs, a family composed of members that are of a number that often
     reflects the size/complexity of the mol. that stimulates their production In
     other words, such responses involve the activation of a polyclonal B
     lymphocyte population. The antibody products of the B cells, although all
     capable of binding the original antigen, bind at various immunogenic sites
     (epitopes) on that antigen. Such differences in antigen-binding fine
     specificity is determined by amino acid residues in the antibody variable
     region domains found associated with the antigen combining site and tend to
     have a complimentary biochem. with the mol. for which they are intended to
     interact. In addition to amino acid differences that dictate the isotypes
     and allotypes of antibody mols., differences in the amino acids that
     compose the variable regions can produce differences in net
     charge of particular antibody mols.; thus, families of polyclonal
     antibodies, all reactive with the same antigen but with different fine
     specificities, can be separated and as shown with acetylcholine
     receptor-reactive antibodies, purified based on their
     isoelec. points by preparative isoelec. focusing (pIEF).
     acetylcholine receptor antibody sepn isoelec focusing
ST
IT
     Isoelectric focusing
        (antibody separation by)
IT
     Antibodies
     RL: PROC (Process)
        (to acetylcholine receptor, separation of, by preparative isoelec. focusing)
IT
     Receptors
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(cholinergic, antibodies to, separation of, by preparative isoelec.

RL: BIOL (Biological study)

focusing)

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ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
     1995:609247 CAPLUS
AN
DN
     123:30814
     Entered STN: 14 Jun 1995
ED
     Purification of antibodies by zeolite A
TI
ΑU
     Huang, Y. C.; Yu, Y. C.; Lee, T. Y.
     Dep. Chem. Eng., Natl. Tsing Hua Univ., Hsinchu, Taiwan
CS
     Enzyme and Microbial Technology (1995), 17(6), 564-9
SO
     CODEN: EMTED2; ISSN: 0141-0229
PB
     Elsevier
     Journal
DT
     English
LA
     15-1 (Immunochemistry)
CC
     Section cross-reference(s): 16
     Zeolite A and its modified forms can be used to sep. IgG from a mixture of
AΒ
     plasma proteins and mouse ascites fluid. The separation was achieved by
     adjusting the pH of buffers according to the isoelec.
     points of proteins in the mixture Zeolite A with potassium cations (K-A)
     and its calcium phosphate modified form (CaP-A) performed better than
     those with sodium, ammonium cations, and dealuminated zeolite X, resp.
     Antibody fractionation eluted from zeolite A columns showed high activity
     and purity, which were verified by SDS-PAGE and ELISA.
     antibody purifn zeolite A
ST
     Ascitic fluid
IT
        (purification of antibodies by ascites fluid by zeolite A and modified
        forms)
IT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (purification of antibodies by ascites fluid by zeolite A and modified
        forms)
·IT
     Antibodies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL .
     (Biological study); PROC (Process)
        (purifn. of antibodies by zeolite A and modified forms)
IT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (A, purification of antibodies by ascites fluid by zeolite A and modified
        forms)
TT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (KA, purification of antibodies by ascites fluid by zeolite A and modified
        forms)
IT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (NH4A, purification of antibodies by ascites fluid by zeolite A and modified
        forms)
IT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (NaA, purification of antibodies by ascites fluid by zeolite A and modified
        forms)
IT
     Zeolites, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (X, purification of antibodies by ascites fluid by zeolite A and modified
IT
     Antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (hepatitis B surface, antibodies to; purification of antibodies by zeolite A
        and modified forms)
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ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
     1995:739415 CAPLUS
AN
DN
     123:141061
ED
     Entered STN: 16 Aug 1995
     Purification of antibody Fab fragments by cation-exchange chromatography
TI
     and pH gradient elution
     Mhatre, R.; Nashabeh, W.; Schmalzing, D.; Yao, X.; Fuchs, M.; Whitney, D.;
ΑU
     Regnier, F.
     PerSeptive Biosystems, 500 Old Connecticut Path, Framingham, MA, 01701,
CS
     Journal of Chromatography, A (1995), 707(2), 225-31
so
     CODEN: JCRAEY; ISSN: 0021-9673
PΒ
     Elsevier
DT
     Journal
     English
LA
CC
     15-1 (Immunochemistry)
AΒ
     The use of a pH gradient as opposed to conventional salt
     gradient for elution in cation-exchange chromatog. was explored.
     PH gradients were very effective in separating Fab fragments and other
    proteins with differences in isoelec. point as low as 0.1. To
     determine the efficiency of purification, the separated peaks were collected
and further
     analyzed by capillary electrophoresis.
     antibody Fab fragment purifn cation chromatog
ST
IT
    Antibodies
    RL: PUR (Purification or recovery); PREP (Preparation)
        (purifn. of antibody Fab fragments by cation-exchange
       chromatog. and pH gradient elution)
     Chromatography, column and liquid
IT
        (cation-exchange, purification of antibody Fab fragments by cation-exchange
        chromatog. and pH gradient elution)
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## (FILE 'HOME' ENTERED AT 09:53:41 ON 19 SEP 2006)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 09:53:59 ON 19 SEP 2006

L1	893 S (ANTIBOD? PURIF?)
L2	6 S L1 AND (NET CHARGE)
L3	327 S L1 AND PH
L4	17 S L3 AND ISOELECTRIC?
L5	0 S L4 AND L2
L6	258 DUPLICATE REMOVE L3 (69 DUPLICATES REMOVED)
L7	258 S L6 AND PH
L8	0 S L2 AND PH
L9	3 DUPLICATE REMOVE L2 (3 DUPLICATES REMOVED)
L10	17 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)